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An unprecedented ortho effect in mass spectrometric fragmentation of even-electron negative ions from hydroxyphenyl carbaldehydes and ketones

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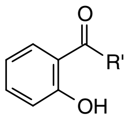
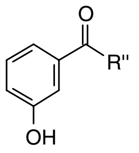
Abstract—A mass spectrometric peak for a carboxylate anion is observed in collision-induced dissociation (CID) mass spectra recorded from negative ions derived from *ortho* isomers of hydroxyphenyl carbaldehydes and ketones. For example, CID spectra of 2-hydroxy derivatives of benzaldehyde, acetophenone, propiophenone, isobutyrophenone, and pivalophenone show peaks at *m*/*z* 45, 59, 73, 87, and 101 for the formate, acetate, propionate, isobutyrate, and pivalate anions, respectively.

It is well known that positive-ion electron ionization mass spectra of *ortho* compounds can be distinguished from those of related *meta* or *para* isomers.[1,2] However, such ortho effects for the prediction of substitution positions from CID mass spectra of even-electron ions have been rarely reported.[3–5] Unlike radical ions generated by electron ionization, electrospray ionization produces even-electron ions such as $[M+H]^+$ or $[M-H]^-$. By examining a large number of CID spectra of negative ions derived from deprotonation of isomers of hydroxybenzaldehydes, hydroxyacetophenones, and hydroxyacetonaphthones under electrospray ionization conditions, we found that unequivocal identifications of the *ortho* isomers can be based solely on their negative ion CID spectra.

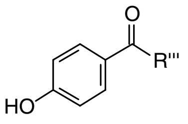
For example, in the negative ion CID spectrum of *ortho*-hydroxybenzaldehyde (**1**), a weak but highly significant peak is observed at *m*/*z* 45 (Fig. 1A). This peak, which is absent in the spectra of *meta* (**6**) and *para* (**11**) isomers of hydroxybenzaldehyde (Fig. 1B and C), represents the formate anion.



1 R' = H
2 R' = $\mathrm{CH_3}$
3 R' = $\mathrm{CH_2CH_3}$
4 R' = $\mathrm{CH(CH_3)_2}$
5 R' = $\mathrm{C(CH_3)_3}$



6 R'' = H
7 R'' = $\mathrm{CH_3}$
8 R'' = $\mathrm{CH_2CH_3}$
9 R'' = $\mathrm{CH(CH_3)_2}$
10 R'' = $\mathrm{C(CH_3)_3}$



11 R''' = H
12 R''' = $\mathrm{CH_3}$
13 R''' = $\mathrm{CH_2CH_3}$
14 R''' = $\mathrm{CH(CH_3)_2}$
15 R''' = $\mathrm{C(CH_3)_3}$

In fact, a more pronounced peak is observed at *m*/*z* 59 for the acetate anion in the spectrum of 2-hydroxyacetophenone (**2**) (Fig. 2A) and that of 2-hydroxyacetonaphthone (Fig. 6A) demonstrating that the elimination of a carboxylate anion in this way is not restricted to hydroxyphenyl carbaldehydes. Moreover, the spectra of 2-hydroxypropiophenone (**3**) (Fig. 2B), 2-hydroxyisobutyrophenone (**4**) (Fig. 2C), and 2-hydroxypivalophenone (**5**) (Fig. 2D) showed peaks at *m*/*z* 73, 87, and 101 for the propionate, isobutyrate and pivalate anions, respectively, suggesting that our observation is a general phenomenon.

We propose that the carboxylate anion observed here is formed via a heterolytic rearrangement involving a four-membered intermediate.

Keywords: ESI-MS; Ortho effect; Collision-induced dissociation (CID); Negative-ion mass spectrometry; Hydroxybenzaldehyde; Hydroxyacetophenone.

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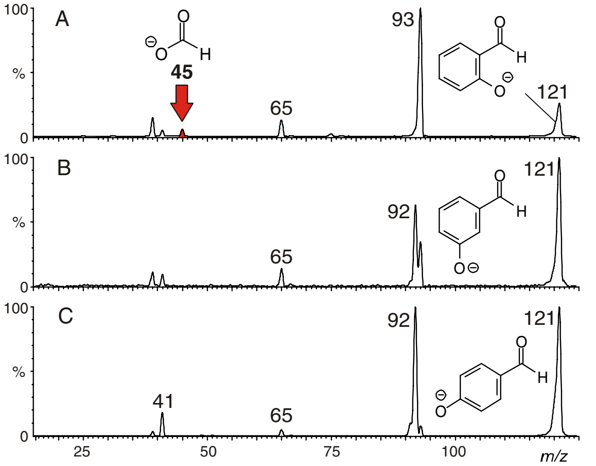


Figure 1. Product ion spectrum of $[M-H]^-$ ion (*m/z* 121) derived from *ortho*-(A), *meta*-(B), and *para*-hydroxybenzaldehyde (C) at a laboratory-frame collision energy setting of 25 eV (all parameters including collision gas pressure and cone voltage were identical).

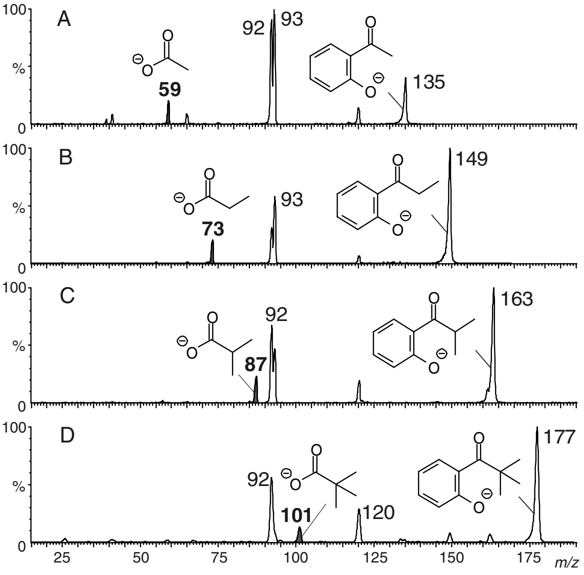
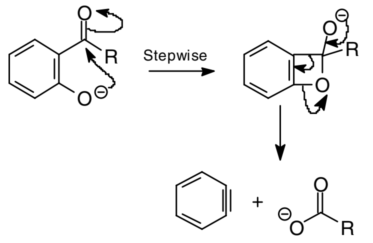


Figure 2. Product ion spectrum of $[M-H]^-$ ion derived from 2-hydroxyacetophenone (*m/z* 135) (A), 2-hydroxypropiophenone (*m/z* 149) (B), 2-hydroxyisobutyrophenone (*m/z* 163) (C), and 2-hydroxypivalophenone (*m/z* 177) (D) (all parameters including collision gas pressure and collision energy were kept identical).

To rationalize the elimination of the carboxylate anion, we propose a charge-mediated mechanism (Scheme 1). In this stepwise mechanism, an internal nucleophilic attack first leads to an oxetane heterocycle, which decomposes to benzyne and a carboxylate anion. To the best of our knowledge, such a formation of a carboxylate anion has not been reported previously in gas phase ion chemistry.

The peak for acetate ion at *m/z* 59 is absent in the spectra of *meta*-(**7**) and *para*-(**12**) isomers of hydroxyacetophenone, confirming that the observed phenomenon is specific to compounds with hydroxyl and acyl substituents on adjacent carbon atoms (Fig. 3B and C).



Scheme 1. Proposed stepwise fragmentation mechanism for the carboxylate ion formation from $[M-H]^-$ of *ortho*-hydroxyphenyl carbaldehydes (R = H) and ketones (R = alkyl).

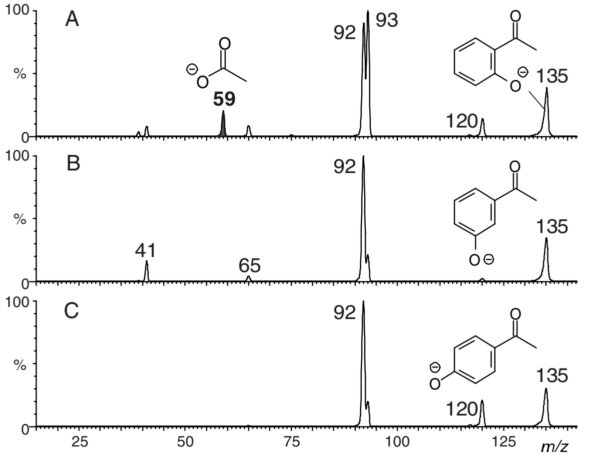


Figure 3. Product ion spectrum of $[M-H]^-$ ion (*m/z* 135) derived from 2-hydroxyacetophenone (A), 3-hydroxyacetophenone (B), and 4-hydroxyacetophenone (C) (all parameters including collision gas pressure and cone voltage were kept identical).

Similarly, a peak at *m/z* 73 for the propionate anion was observed only in the spectrum of *ortho* isomer of hydroxypropiophenone (**3**) (Fig. 4).

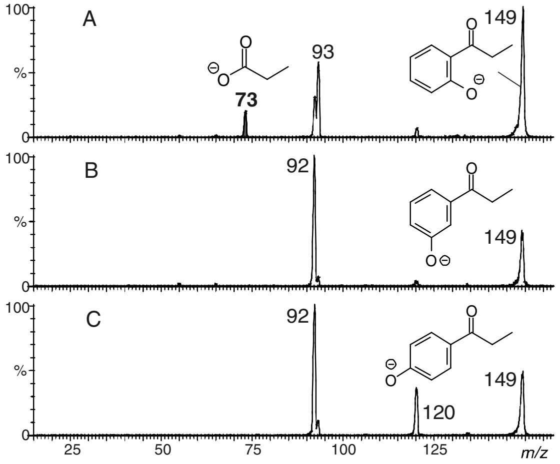


Figure 4. Product ion spectrum of $[M-H]^-$ ion (*m/z* 149) derived from 2-hydroxypropiophenone (A), 3-hydroxypropiophenone (B), and 4-hydroxypropiophenone (C) (all parameters including collision gas pressure and collision energy were kept identical).

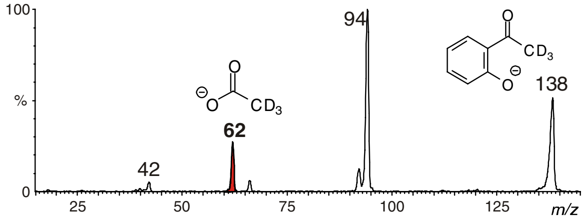


Figure 5. Product ion spectrum of $[M-H]^-$ (*m*/*z* 138) ion derived from 2-hydroxy-[2′,2′,2′-$^{2}H_{3}$]acetophenone.

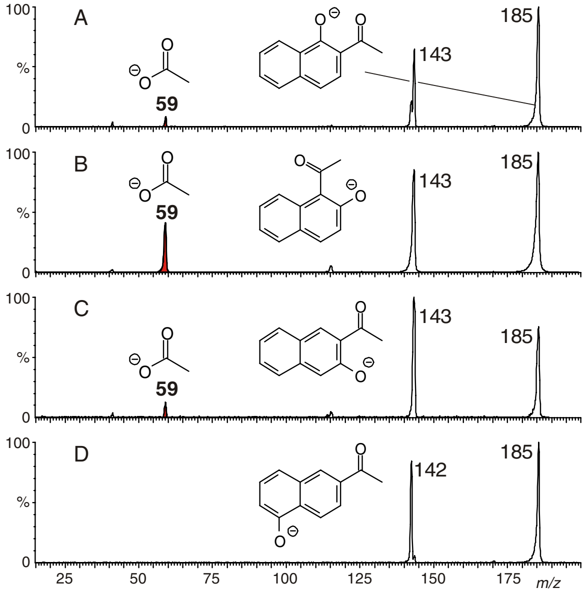


Figure 6. Product ion spectrum of $[M-H]^-$ (*m*/*z* 185) ion derived from 1-hydroxy-2-acetonaphthone (A), 2-hydroxy-1-acetonaphthone (B), 3-hydroxy-2-acetonaphthone (C), and 5-hydroxy-2-acetonaphthone (D) (all parameters including collision gas pressure and collision energy were kept identical).

The proposed mechanism is further supported by the observation that the spectrum of 2-hydroxy-[2′,2′,2′-$^{2}H_{3}$]acetophenone showed the corresponding peak at *m*/*z* 62 for acetate-d_3 anion (Fig. 5).

Spectra recorded from several isomers of hydroxyacetonaphthone confirmed that the 1,2-relationship of the hydroxyl and acyl groups is an absolute prerequisite for the proposed mechanism (Fig. 6) to operate. For example, the spectrum of 5-hydroxy-2-acetonaphthone is devoid of a *m*/*z* 59 peak (Fig. 6D).

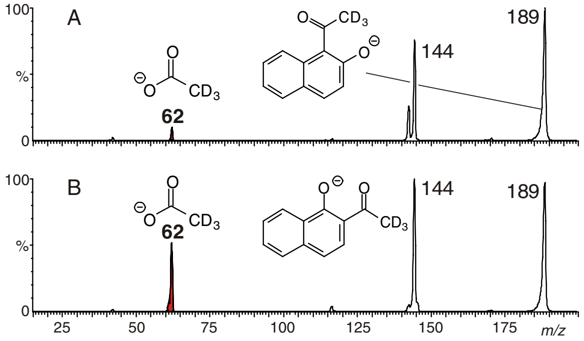


Figure 7. Product ion spectrum of $[M-H]^-$ ion (*m*/*z* 189) derived from 1-hydroxy-2-[2′,2′,2′-$^{2}H_{3}$]acetonaphthone (A) and 2-hydroxy-1-[2′,2′,2′-$^{2}H_{3}$]acetonaphthone (B) (all parameters including collision gas pressure and collision energy were kept identical).

Moreover, the spectra of 1-hydroxy-2-[2′,2′,2′-$^{2}H_{3}$]acetonaphthone and 2-hydroxy-1-[2′,2′,2′-$^{2}H_{3}$]acetonaphthone showed peaks at *m*/*z* 62, confirming that the transfer of the oxygen atom requires the 1,2-relationship (Fig. 7).

In summary, the presence or absence of a peak for the carboxylate anion can be used to determine the positional relationship between hydroxyl and acyl groups in hydroxyphenyl carbaldehydes, ketones and their derivatives. Further research is in progress to establish the fragmentation mechanism governing this unprecedented 1,2-elimination reaction.

Acknowledgement

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References and notes

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